Comparison of Estimated PCB-153 Concentrations in Human Milk Using Various Pharmacokinetic Models

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Risk to infants from consuming human milk contaminated with lipophilic chemicals is difficult to assess. Typically, risk assessors use measured chemical concentrations in media of concern. Human milk is often difficult to sample for chemical concentrations. Therefore, models that predict chemical levels in human milk and subsequent average daily dose to the nursing infant (ADDi) are desirable. We compared adaptations of three published models in an effort to help risk assessors and public health practitioners choose an appropriate method to estimate ADDi. Models chosen for comparison included a classic single-compartment model, a 3-compartment physiologically-based pharmacokinetic (PBPK) model, and an 8-compartment PBPK model. The models were compared by running two sets of simulations in each model using the polychlorinated biphenyl congener 153 (PCB-153), a lipophilic environmental contaminant. The first set of simulations used back-calculated average maternal daily oral dose (ADDm) values as starting points. ADDm was calculated using the 8-compartment PBPK model based on PCB-153 blood concentrations measured in 8 human subjects. From derived ADDm values, the models simulated both the milk concentration and ADDi for each subject. Estimated milk concentrations were then compared to observed concentrations. The second set of simulations used an ADDm derived for PCB-153 assuming consumption of contaminated fish. All 3 model results were similar to within a factor of 2. The classic single compartment model consistently produced the highest estimates of PCB-153 concentration in human milk and ADDi. Our results indicate that the simplest model studied may be appropriate for risk assessors and public health practitioners to use for predicting the ADDi for lipophilic environmental contaminants.

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